Impact of Final Kissing Balloon Inflation or Two-stent Technique for Bifurcation Coronary Lesions

CROSS and PERFECT Trials

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Disclosure

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  - CardioVascular Research Foundation (CVRF)
  - Korean Society of Interventional Cardiology
  - Korea Healthcare technology R&D Project, Ministry of Health and Welfare

Current RCTs for Bifurcation Lesions

No Difference of Outcomes

Trials	Comparison
NORDIC 1	Provisional T vs. Systemic T stenting
NORDIC 2	Crush vs. Culotte
NORDIC 3	Kissing balloon vs. leave alone
BBC	Simple vs. Complex
CACTUS	Provisional T vs. Crush

Lessons From Trials

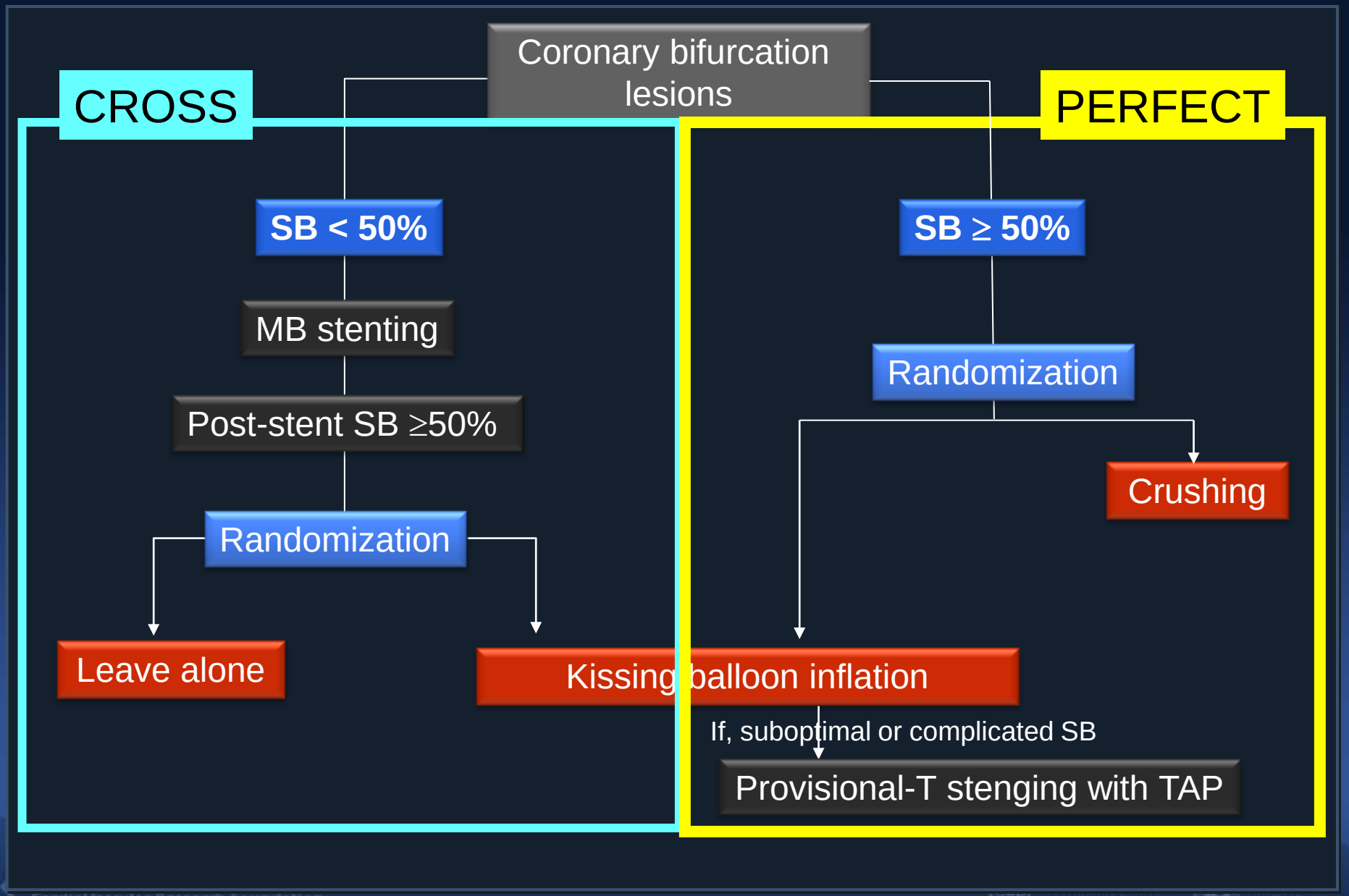
- No difference in the rate of death, spontaneous MI, and repeat revascularization rate
- Superiority of 1-stent technique in the rate of periprocedural MI
- Low cost and simple procedure for 1-stent

BUT, limited by selected inclusion, heterogeneous bifurcations, different procedures, and angiography-guidance

Purpose of CROSS and PERFECT Trials

To compare outcomes of two different techniques for patients with bifurcation stenosis stratified by the presence of SB stenosis.

CROSS & PERFECT Trials



Administration and Sites

Sites

Asan Medical Center

Aju University Hospital

Busan Saint Mary's Hospital

Busan University Hospital

Catholic University, Kangnam St. Mary's Hospital

Chungju Saint Mary's Hospital

Chungnam National University Hospital

Hallym University Sacred Heart Hospital

Kangwon University Hospital

Korea Veterans Hospital

Kyungsang University Hospital

Soonchunhyang University Seoul Hospital

Soonchunhyang University Bucheon Hospital

Soonchunhyang University Cheonan Hospital

Ulsan University Hospital

Principle investigator

Seung-Jung Park, MD, PhD

Angiographic and IVUS Core Lab

Data management

Clinical Event Committee

Data Safety Monitoring Board

CardioVascular Research Foundation, Seoul, Korea

Inclusion Criteria

1. Clinical

- Ischemic symptom or sign
- Eligible lesion for intracoronary stenting
- Age >18 years, <75 ages

2. Angiographic

- De novo bifurcation
- **MB:** ≥ 2.5 mm, ≥ 50% stenosis, ≤ 50 mm length covered with ≤ 2 stents
- **SB:** ≥ 2.0 mm, < 50% stenosis (CROSS)
- **SB:** ≥ 2.0 mm, ≥ 50% & < 20 mm length (PERFECT)

Exclusion Criteria

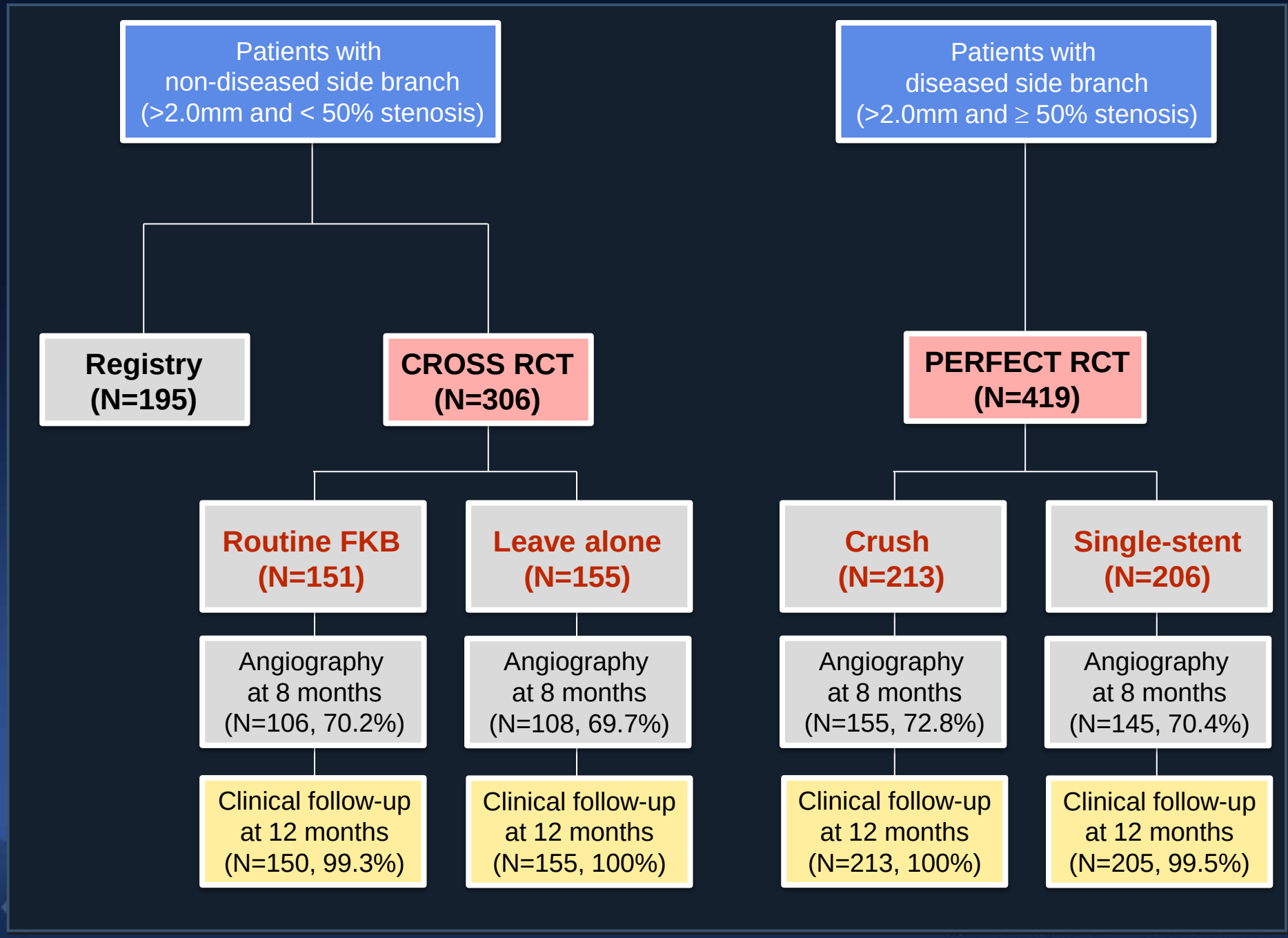
- Serious comorbidity with left expectancy < 1 year
- STEMI ≤ 2 weeks
- LM disease
- In-stent restenosis
- Graft vessels
- TIMI flow ≤ grade 2 in the side branch
- CTO
- Renal dysfunction, Creatinine ≥ 2.0 mg/dL

Primary End Points
Angiographic Surrogates

- **CROSS**
  - Non-inferiority design
  - 8-month % diameter stenosis in analysis segment of SB
- **PERFECT**
  - Superiority design (crush is better)
  - 8-month overall restenosis rate

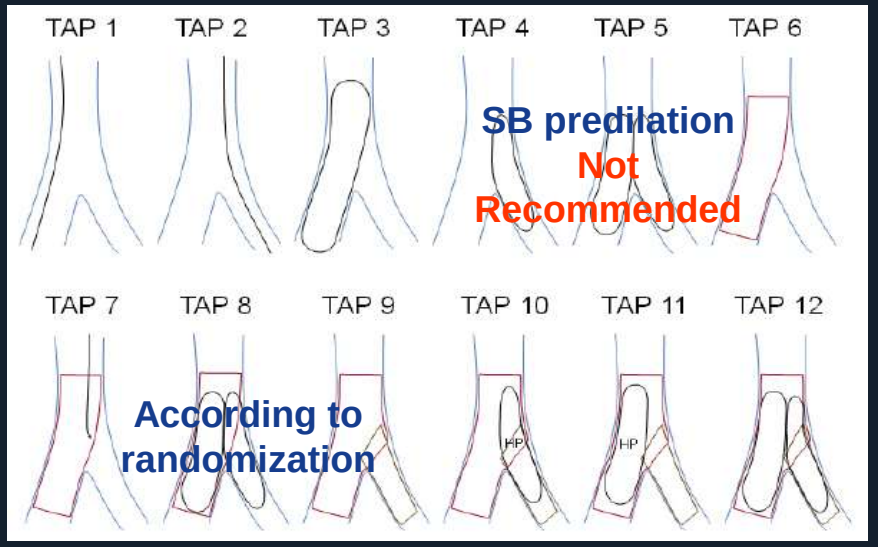
Clinicaltrialgov.com, NCT00694005

Clinicaltrialgov.com, NCT00693251

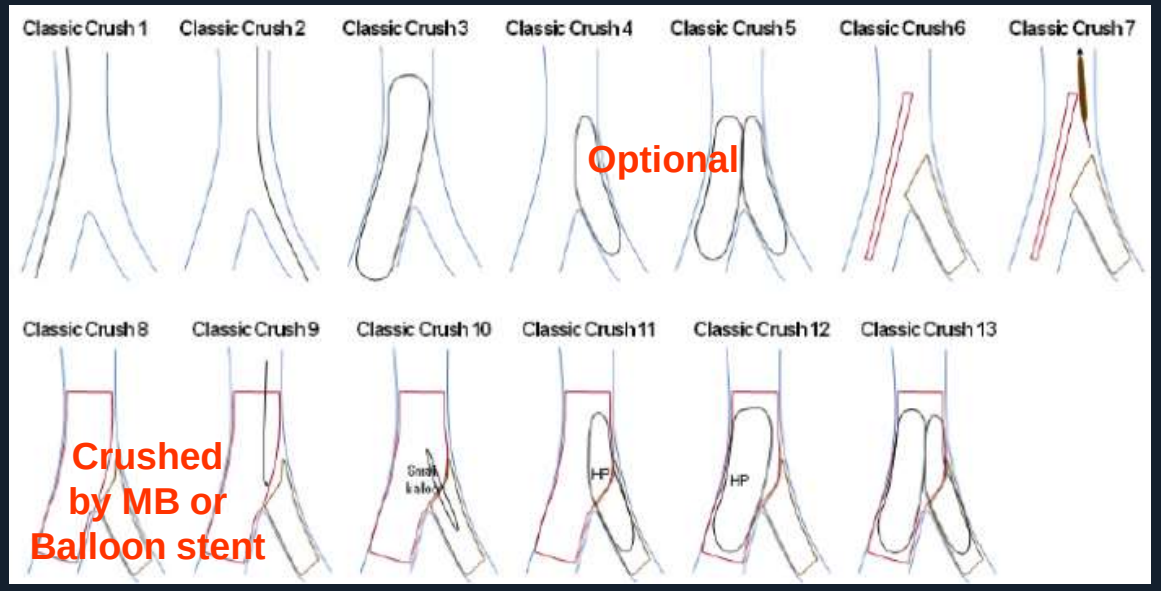


Prespecification and Consensus on Procedural Steps

Single-stent with
Routine FKB or selective FKB
Or optional Provisional-T



Crush
with balloon or
stent crush



Baseline Characteristics

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=151)	Leave-alone (N=155)	P	Crush (N=213)	1-stent (N=206)	P
Age, years	61.0±9.2	61.0±7.9	0.98	60.9±8.9	61.1±8.8	0.86
Male	107 (70.9)	104 (67.1)	0.48	160 (75.1)	155 (75.2)	1.0
BMI, kg/m^2	24.7±3.0	24.9±2.6	0.75	24.9±2.8	24.9±3.0	0.86
Current smoking	50 (33.1)	39 (25.2)	0.13	54 (25.4)	67 (32.5)	0.11
Diabetes mellitus	46 (30.5)	45 (29.0)	0.78	55 (25.8)	60 (29.1)	0.45
Hypertension	84 (55.6)	91 (58.7)	0.59	118 (55.4)	114 (55.3)	0.99
Hyperlipidemia	71 (47.0)	77 (49.7)	0.64	132 (62.0)	118 (57.3)	0.33
Family history	10 (6.6)	19 (12.3)	0.092	30 (14.1)	26 (12.6)	0.66
Prior CABG	8 (5.3)	15 (9.7)	0.15	20 (9.4)	11 (5.3)	0.11

Baseline Characteristics

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=151)	Leave-alone (N=155)	P	Crush (N=213)	1-stent (N=206)	P
CRF	4 (2.6)	0	0.058	1 (0.5)	1 (0.5)	1.0
CHF	0	0		0	2 (1.0)	0.24
Prior MI	3 (2.0)	6 (3.9)	0.5	9 (4.2)	9 (4.4)	0.94
Clinical symptom			0.64			0.43
Stable	74 (49.0)	84 (54.2)		130 (61.3)	127 (62.0)	
Unstable angina	66 (43.7)	62 (40.0)		74 (34.9)	65 (31.7)	
Recent MI	11 (7.3)	9 (5.8)		8 (3.8)	13 (6.3)	
LVEF, %	60.9 ± 7.0	62.2 ± 5.7	0.098	60.4 ± 6.8	59.5 ± 7.2	0.2

Procedures

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=151)	Leave-alone (N=155)	P	Crush (N=213)	1-stent (N=206)	P
Treated vessels			0.54			0.62
1 vessel	111 (73.5)	109 (70.3)		159 (74.6)	145 (70.4)	
2 vessels	35 (23.2)	43 (27.7)		46 (21.6)	52 (25.2)	
3 vessels	5 (3.3)	3 (1.9)		8 (3.8)	9 (4.4)	
Target lesions			0.69			0.33
LAD	137 (90.7)	137 (88.4)		200 (93.9)	190 (92.2)	
LCX	11 (7.3)	12 (7.7)		10 (4.7)	15 (7.3)	
RCA	3 (2.0)	6 (3.9)		3 (1.4)	1 (0.5)	
Trans-radial	56 (37.1)	55 (35.5)	0.77	25 (11.7)	25 (12.1)	0.90
Procedure T, min	40.8±18.5	32.8 ± 16.2	< 0.001	52.5±21.0	48.7±21.2	0.065
Fluoroscopic T, min	21.4±10.3	17.9 ± 8.1	0.001	29.3±14.1	25.9±12.7	0.013
Contrast, cc	287±128	273± 110	0.31	350±145	347±125	0.85

Procedures for Main Branch

Variables	CROSS Study			PERFECT Study		
	Routine-FKB	Leave-alone	P	Crush	1-stent	P
NC balloon	95 (62.9)	87 (56.1)	0.23	141 (66.2)	97 (47.1)	< 0.001
Cutting balloon	0	1 (0.6)	1.00	6 (2.8)	2 (1.0)	0.29
IVUS	139 (92.1)	149 (96.1)	0.13	204 (95.8)	197 (95.6)	0.94
Predilation	148 (98.0)	149 (96.1)	0.50	208 (97.7)	202 (98.1)	1.0
Stents	151 (100)	155 (100)		213 (100)	206 (100)	
Number	1.3±0.5	1.2±0.4	0.61	1.4±0.5	1.4±0.5	0.76
Diameter, mm	3.5±2.2	3.3±0.3	0.23	3.3±0.3	3.3±0.3	0.49
Length, mm	33.2±13.1	33.0±14.8	0.94	37.3±14.7	36.9±15.3	0.76
Maximal Pr, atm	19.2±4.4	18.5±4.6	0.18	18.7±4.1	15.9±4.7	< 0.001
Used stents			0.58			0.98
SES	47 (31.1)	36 (23.2)		127 (59.6)	118 (57.3)	
PES	17 (11.3)	21 (13.5)		2 (0.9)	3 (1.5)	
EES	33 (21.9)	36 (23.2)		59 (27.7)	59 (28.6)	
ZES	44 (29.1)	53 (34.2)		19 (8.9)	19 (9.2)	
Others	10 (6.6)	9 (5.8)		6 (2.8)	7 (3.4)	

Procedures for Side Branch

Variables	CROSS Study			PERFECT Study		
	Routine-FKB	Leave-alone	P	Crush	1-stent	P
NC balloon	18 (11.9)	2 (1.3)	< 0.001	116 (54.5)	26 (12.6)	< 0.001
Cutting balloon	0	1 (0.6)	1.00	2 (0.9)	0	0.50
IVUS	73 (48.3)	51 (32.9)	0.006	195 (91.5)	164 (79.6)	< 0.001
Predilation	5 (3.3)	6 (3.9)	0.79	177 (83.1)	76 (36.9)	< 0.001
Stent	3 (2.0)	1 (0.6)	0.37	208 (97.7)	58 (28.2)	< 0.001
Number	1	1	-	1.0 ± 0.2	1.0 ± 0.2	0.66
Diameter, mm	2.6±0.1	2.8	0.42	2.7±0.2	2.7±0.2	1.00
Length, mm	24.7±2.9	30.0	0.25	21.4±6.7	21.5±6.9	0.93
Max. Pr, atm	15.7±5.1	17.0	0.84	18.0±4.2	15.1±4.0	< 0.001
Used stents			0.50			0.85
SES	2 (66.7)	0		126 (60.6)	34 (58.6)	
PES	0	0		2 (1.0)	0	
EES	1 (33.3)	0		54 (26.0)	19 (32.8)	
ZES	0	1 (100)		18 (8.7)	4 (6.9)	
Others	0	0		8 (3.8)	1 (1.7)	

SB Stenting Techniques

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=151)	Leave-alone (N=155)	P	Crush (N=213)	1-stent (N=206)	P
FKB	144 (95.4)	7 (4.5)	< 0.001	204 (95.8)	163 (79.1)	< 0.001
Stent	3 (2.0)	1 (0.6)	0.37	208 (97.7)	58 (28.2)	< 0.001
Stenting technique			0.75			< 0.001
Crush	0	0		206 (99.0)	15 (25.9)	
Provisional T	2 (66.7)	1 (100)		1 (0.5)	43 (74.1)	
Others	1 (33.3)	0		1 (0.5)	0	

Medina Classification in Core Lab

Variables	CROSS Study			PERFECT Study		
	Routine-FKB	Leave-alone	P	Crush	1-stent	P
Medina class			0.18			0.012
1. 0. 0.	18 (12.2)	15 (9.8)		2 (1.0)	4 (2.0)	
1. 1. 0.	52 (35.1)	74 (48.4)		5 (2.4)	22 (10.9)	
1. 0. 1.	8 (5.4)	4 (2.6)		18 (8.7)	18 (8.9)	
1. 1. 1.	28 (18.9)	24 (15.7)		137 (65.9)	126 (62.4)	
0. 1. 0.	34 (23.0)	25 (16.3)		4 (1.9)	5 (2.5)	
0. 1. 1.	6 (4.1)	4 (2.6)		39 (18.8)	25 (12.4)	
0. 0. 1.	1 (0.7)	3 (2.0)		3 (1.4)	2 (1.0)	
0. 0. 0.	1 (0.7)	4 (2.6)		0	0	
SB stenosis	**29.1%**	**22.9%**		**94.8%**	**84.7%**	

Angiography after Procedure

Variables	CROSS Study			PERFECT Study		
	Routine-FKB	Leave-alone	P	Crush	1-stent	P
Main branch						
Stent length, mm	31.5±12.0	30.9±11.7	0.66	34.0±13.5	34.7±13.4	0.64
MLD, mm						
In-stent	2.6±0.4	2.6±0.4	0.68	2.6±0.4	2.7±0.4	0.041
In-segment	2.2±0.4	2.2±0.4	0.53	2.2±0.4	2.3±0.5	0.13
DS, %						
In-stent	11.6±6.6	12.8±7.2	0.12	13.5±7.2	13.0±6.9	0.48
In-segment	20.3±8.7	20.7±8.3	0.70	22.1±10.0	20.7±8.7	0.12
Side branch						
Stent length, mm	15.3±8.1	24.6	0.42	15.4±7.1	16.4±6.6	0.32
MLD ostium, mm	1.7±0.4	1.6 ± 0.5	0.053	2.3±0.4	1.9±0.6	< 0.001
DS ostim, %	25.8±15.0	32.2 ± 18.2	0.001	13.7±11.1	25.7±17.8	< 0.001

Main Brach Follow-up Angiography

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=106)	Leave-alone (N=108)	P	Crush (N=155)	1-stent (N=145)	P
MLD, mm						
In-stent	2.2±0.6	2.3±0.5	0.32	2.4±0.4	2.4±0.5	1.0
In-segment	1.9±0.6	2.1±0.4	0.071	2.1±0.4	2.2±0.5	0.44
DS, %						
In-stent	22.8±16.2	20.5±13.4	0.24	19.8±10.6	21.3±13.3	0.26
In-segment	29.7±17.3	25.7±13.1	0.064	26.8±13.1	26.1±12.4	0.65
Late loss, mm						
In-stent	0.4±0.5	0.3±0.4	0.13	0.2±0.3	0.3±0.4	0.036
In-segment	0.2±0.5	0.1±0.4	0.094	0.1±0.4	0.2±0.4	0.24
Restenosis	16 (15.1)	4 (3.7)	0.004	8 (5.2)	7 (4.8)	0.90
Restenosis pattern			1.0			1.0
Focal	10 (62.5)	2 (50.0)		5 (62.5)	4 (57.1)	
Diffuse	6 (37.5)	2 (50.0)		3 (37.5)	3 (42.9)	

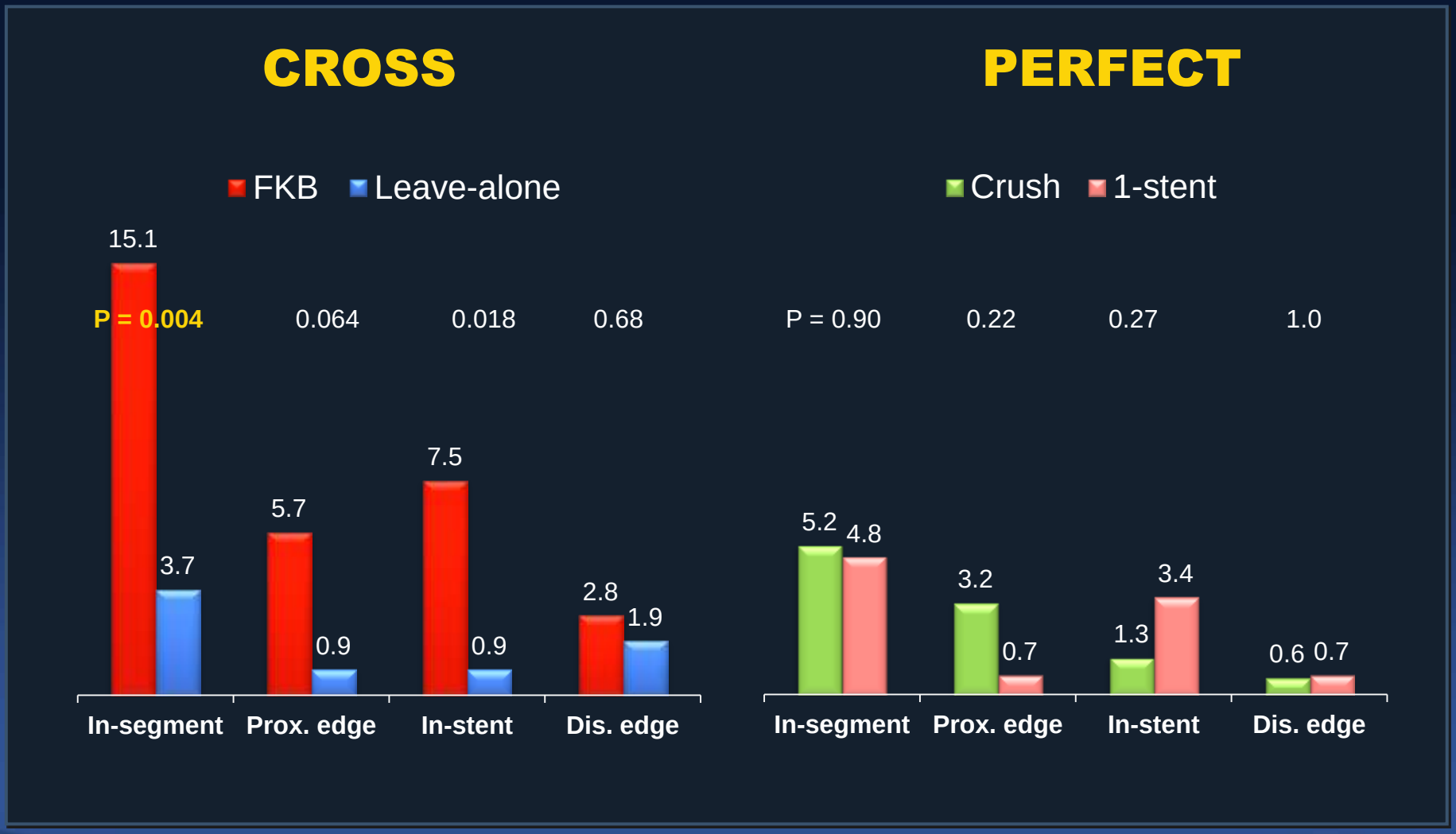
Side Branch Angiographic Follow-up

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=106)	Leave-alone (N=108)	P	Crush (N=155)	1-stent (N=145)	P
MLD, mm						
Ostium	1.6±0.4	1.5±0.5	0.17	2.0±0.4	1.6±0.5	< 0.001
In-segment	1.5±0.4	1.5±0.4	0.73	1.7±0.4	1.4±0.4	< 0.001
DS, %						
Ostium	27.5±15.9	33.3±16.9	0.010	23.2±15.1	34.3±18.9	< 0.001
In-segment	31.1±14.5	34.9±15.8	0.074	27.7±13.2	37.7±17.1	< 0.001
Late loss, mm						
Ostium	0.1±0.4	0.1±0.4	0.59	0.3±0.4	0.3±0.5	0.15
In-segment	0.1±0.4	0.1±0.4	0.88	0.1±0.3	0.2±0.3	0.36
Restenosis	3 (2.8)	6 (5.6)	0.50	6 (3.9)	12 (8.3)	0.12
Pattern			0.33			0.52
Focal	2 (66.7)	6 (100)		6 (100)	9 (75.0)	
Diffuse	1 (33.3)	0		0	3 (25.0)	

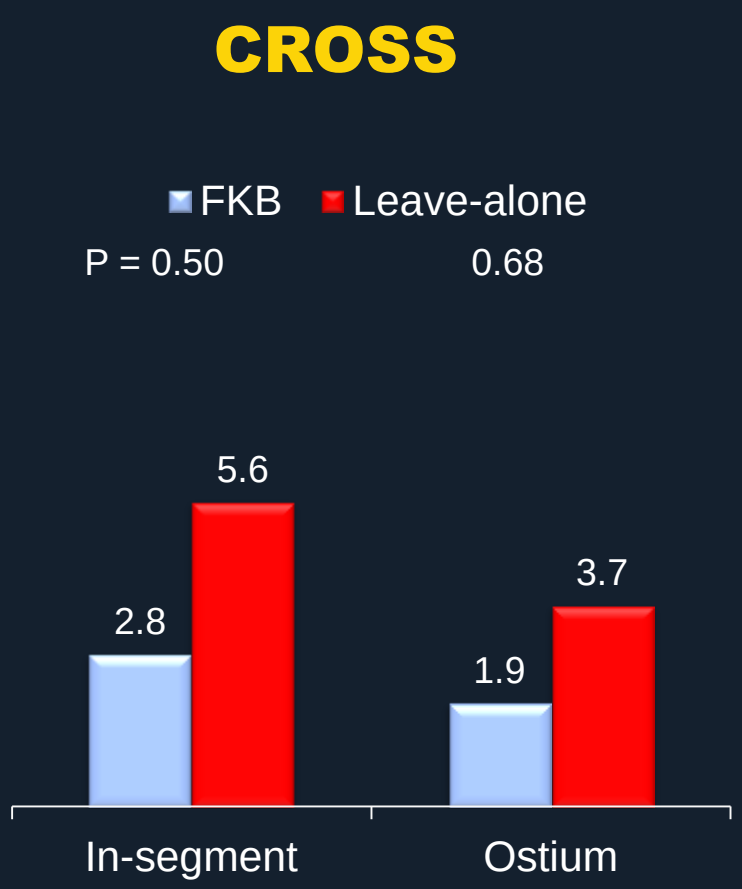
Angiographic Primary End Points

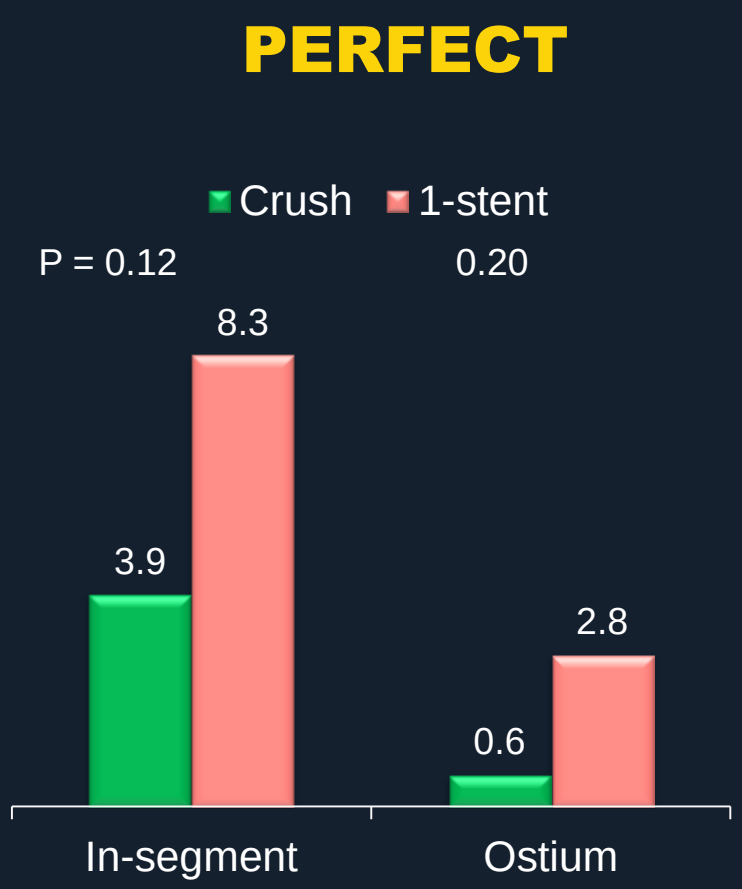
- CROSS study: SB in-segment % DS
  - 31.1±14.5 % in the routine FKB group
  - 34.9±15.8 % in the leave alone group
  - Non-inferiority $p < 0.001$
  - Superiority $p = 0.074$
- PERFECT study: overall restenosis rate
  - 8.4% in the crush group
  - 11.0% in the single-stent group
  - P=0.44

Restenosis of Main Branch

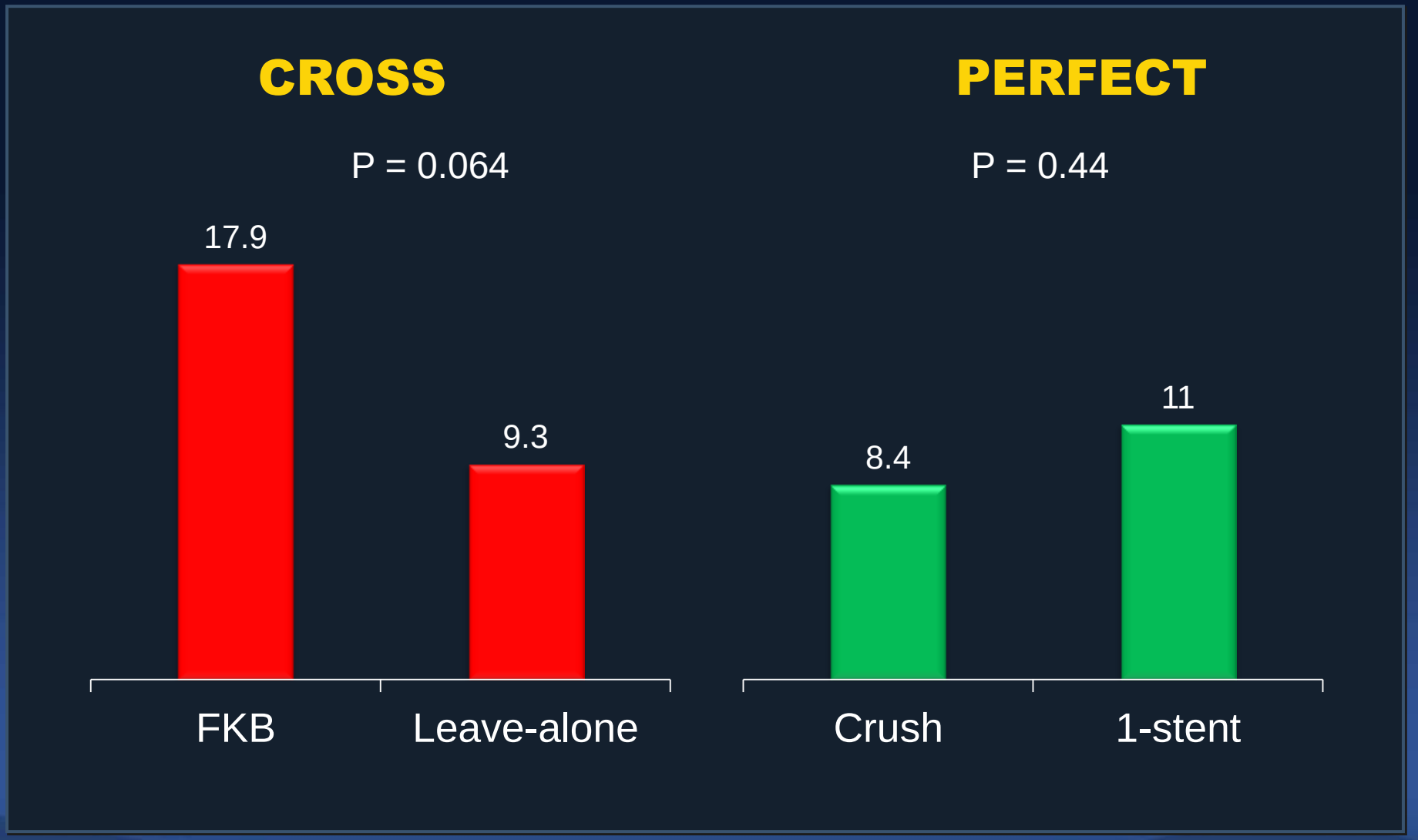


Restenosis of Side Branch





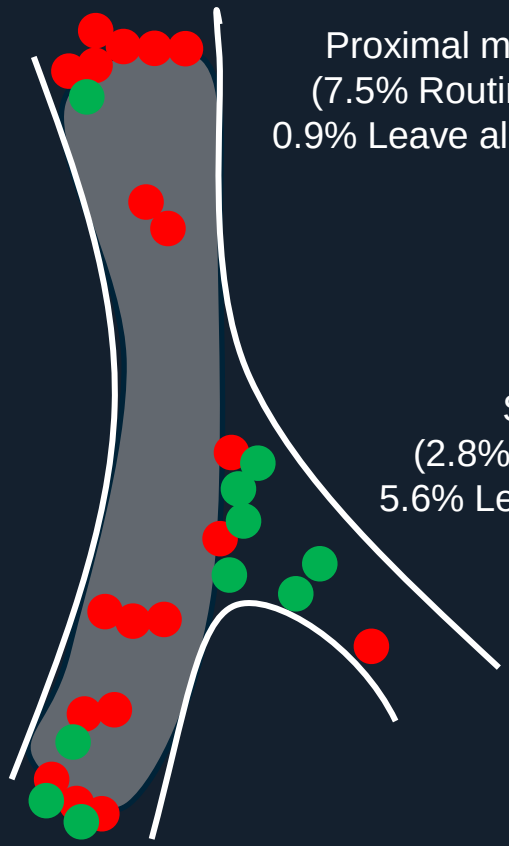
Overall Restenosis Rate



Sites of restenosis

CROSS

Routine-FKB Leave alone



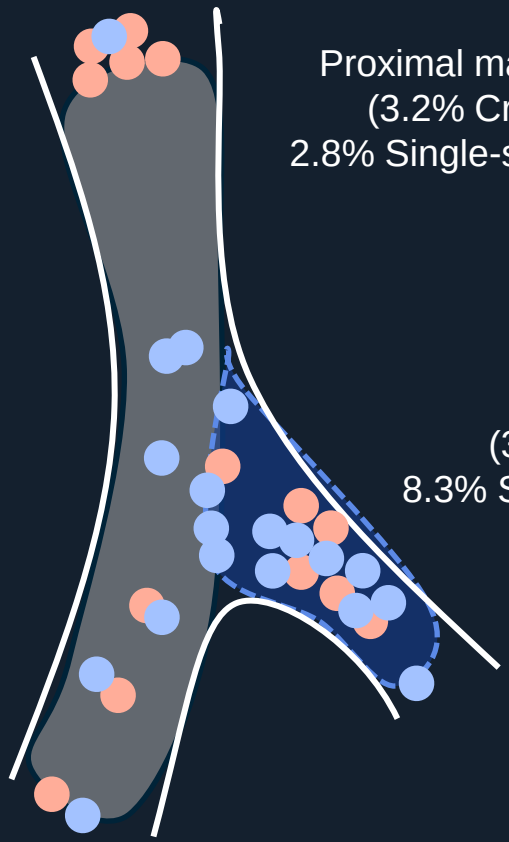
Proximal main branch
(7.5% Routine-FKB vs.
0.9% Leave alone, p=0.018)

Side branch
(2.8% Routine-FKB vs.
5.6% Leave alone, p=0.50)

Distal main branch
(7.5% Routine-FKB vs.
2.8% Leave alone, p=0.11)

PERFECT

Crush Single-stent



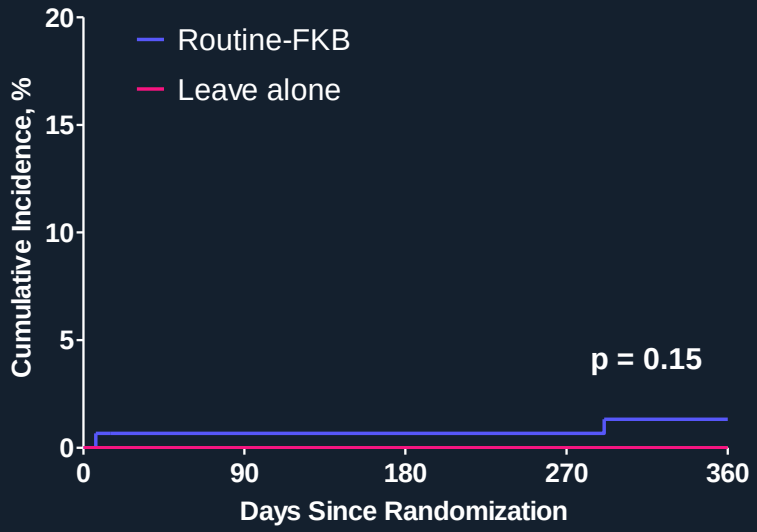
Proximal main branch
(3.2% Crush vs.
2.8% Single-stent, p=1.0)

Side branch
(3.9% Crush vs.
8.3% Single-stent, p=0.11)

Distal main branch
(1.9% Crush vs.
2.1% Single-stent, p=1.0)

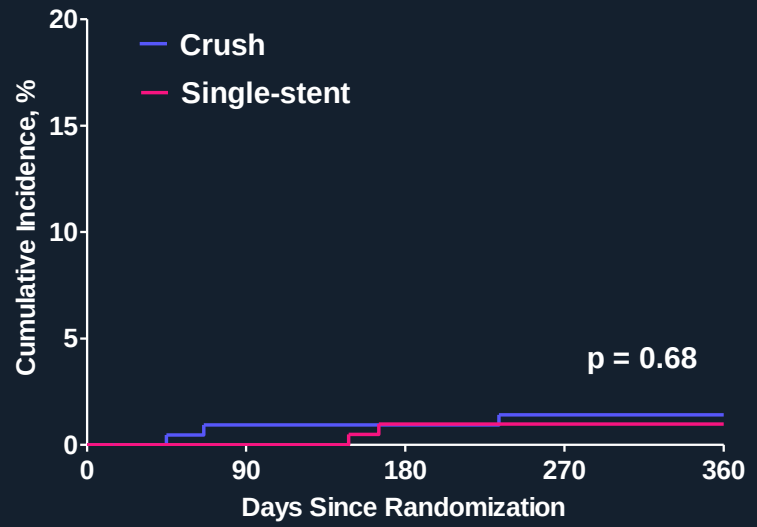
DEATH at 12 months

CROSS



No. at risk					
Routine-FKB	151	150	150	150	148
Leave alone	155	155	155	155	155

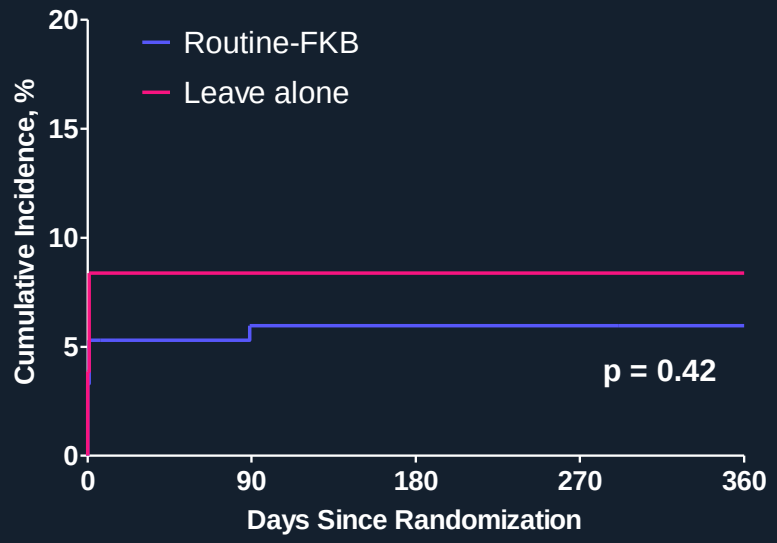
PERFECT



No. at risk					
Crush technique	213	212	212	211	210
Single-stent	206	206	204	204	203

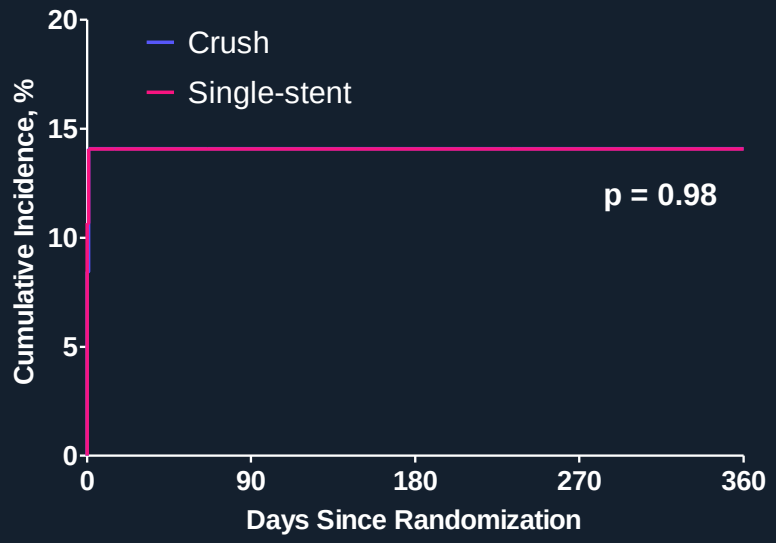
MI at 12 months

CROSS



No. at risk					
Routine-FKB	151	141	141	141	139
Leave alone	155	149	149	149	142

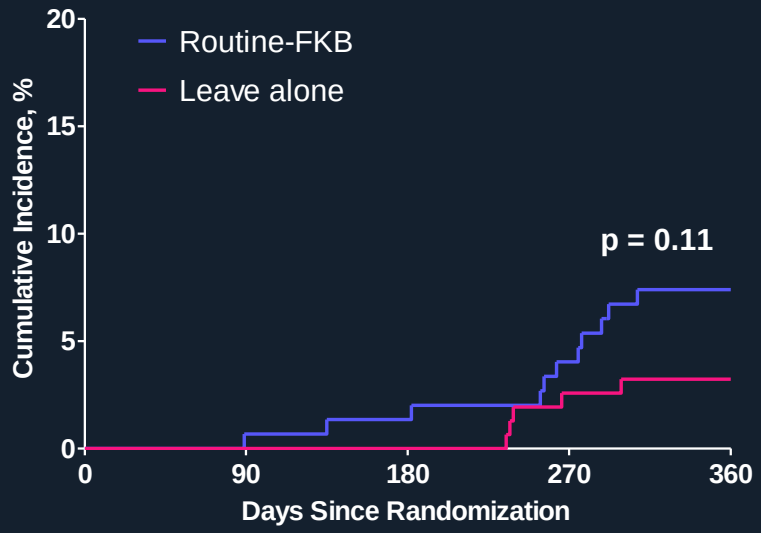
PERFECT



No. at risk					
Crush technique	213	182	182	181	180
Single-stent	206	177	175	175	174

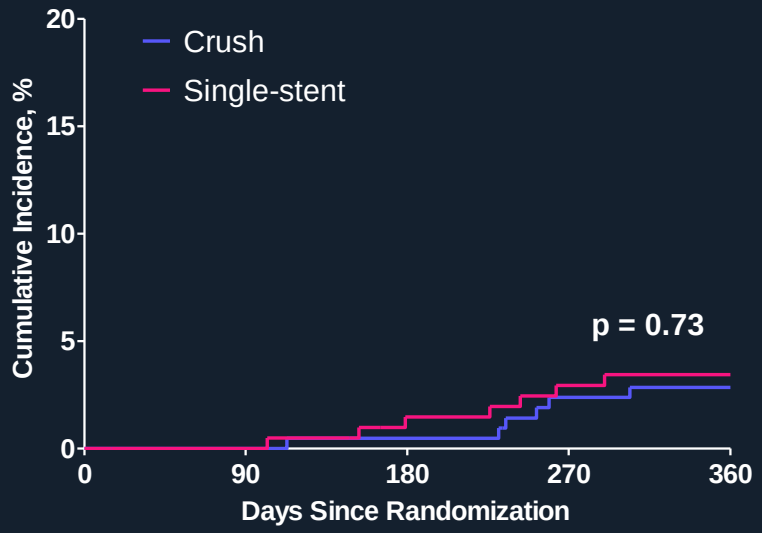
TVR at 12 months

CROSS



No. at risk					
Routine-FKB	151	149	148	144	137
Leave alone	155	155	155	152	150

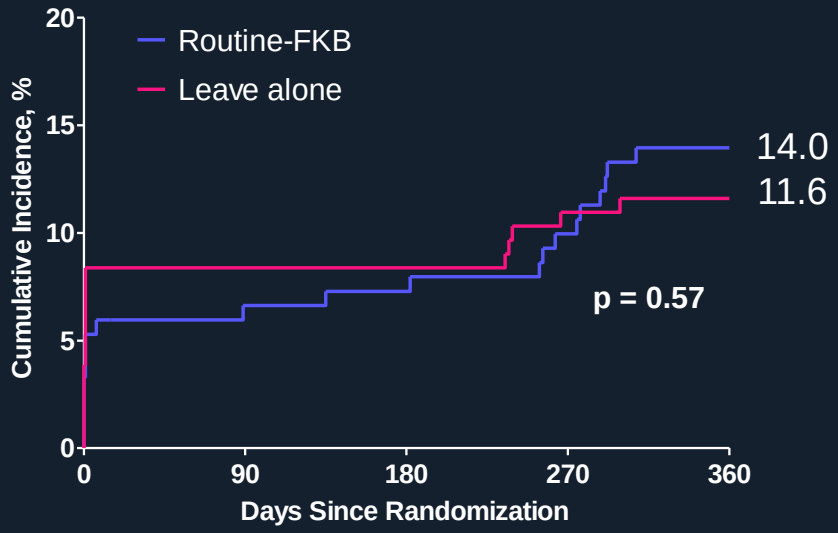
PERFECT



No. at risk					
Crush technique	213	212	211	206	204
Single-stent	206	206	201	198	196

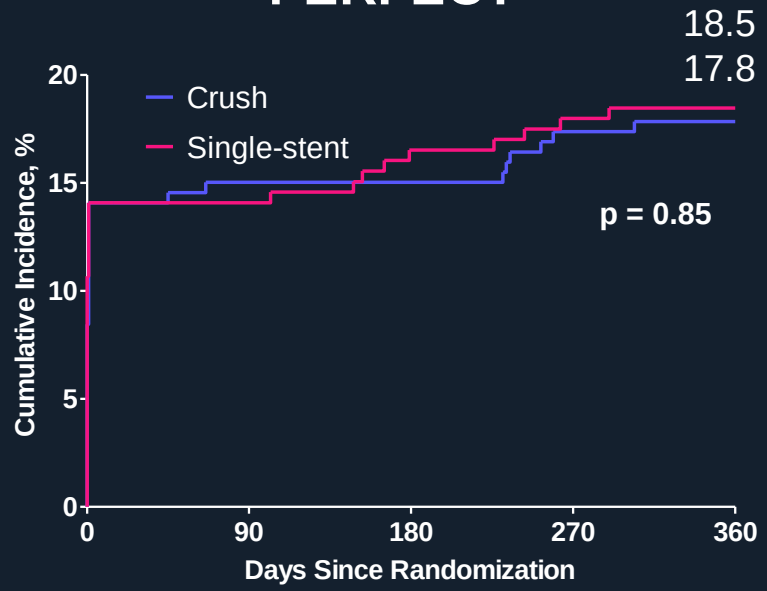
MACE at 12 months

CROSS



No. at risk					
Routine-FKB	151	141	140	136	129
Leave alone	155	149	149	139	137

PERFECT



No. at risk					
Crush technique	213	182	182	177	175
Single-stent	206	177	172	169	167

1-Year Clinical Outcomes

Variables	CROSS Study			PERFECT Study		
	Routine-FKB (N=151)	Leave-alone (N=155)	P	Crush (N=213)	1-stent (N=206)	P
Death	2 (1.3)	0	0.15	3 (1.4)	2 (1.0)	0.68
Cardiac	2 (1.3)	0	0.15	2 (0.9)	1 (0.5)	0.58
Non-cardiac	0	0		1 (0.5)	1 (0.5)	0.98
MI	9 (6.0)	13 (8.4)	0.42	30 (14.1)	29 (14.1)	0.98
Q-wave	0	1 (0.6)	0.32	0	0	
Non-Q wave	9 (6.0)	12 (7.7)	0.55	30 (14.1)	29 (14.1)	0.98
TVR	11 (7.4)	5 (3.2)	0.11	6 (2.9)	7 (3.4)	0.73
Clinically-driven	4 (2.7)	1 (0.6)	0.16	1 (0.5)	3 (1.5)	0.30
TLR	10 (6.7)	4 (2.6)	0.088	4 (1.9)	7 (3.4)	0.33
PCI	10 (6.7)	4 (2.6)	0.088	4 (1.9)	6 (2.9)	0.48
CABG	0	0		0	1 (0.5)	0.31
Stent thrombosis	0	1 (0.6)	0.33	1 (0.5)	0	0.32
MACE	21 (14.0)	18 (11.6)	0.57	38 (17.8)	38 (18.5)	0.85

Conclusions

- This study has strengths: (1) inclusion of all consecutive non-LM bifurcations separated into the two cohorts according to the presence of SB stenosis (2) prespecification of procedural steps (3) treatment using new-generation DES and (4) extensive use of IVUS during treatment.

- The primary finding is that any bifurcation stenting using current DES can achieve excellent long-term prognosis once the procedure is performed successfully.

Conclusion

- In the CROSS study, the selective FKB was not inferior to the routine FKB to treat non-LM bifurcations without SB stenosis in terms of angiographic and clinical outcomes.
- Instead, the strategy of routine FKB was associated with more frequent MB restenosis. This finding indicates that routine FKB is not beneficial but potentially harmful for bifurcations without initial SB stenosis.
- In the PERFCT study, the crush technique failed to achieve better angiographic or clinical outcomes than the single-stent strategy for non-LM bifurcations with SB stenosis.
- It should be noted, however, that a third of patients assigned to the single-stent group finally received SB stents. This finding indicates that the two-stent technique is still required in a group of patients with true bifurcation lesions.

Thank you very much